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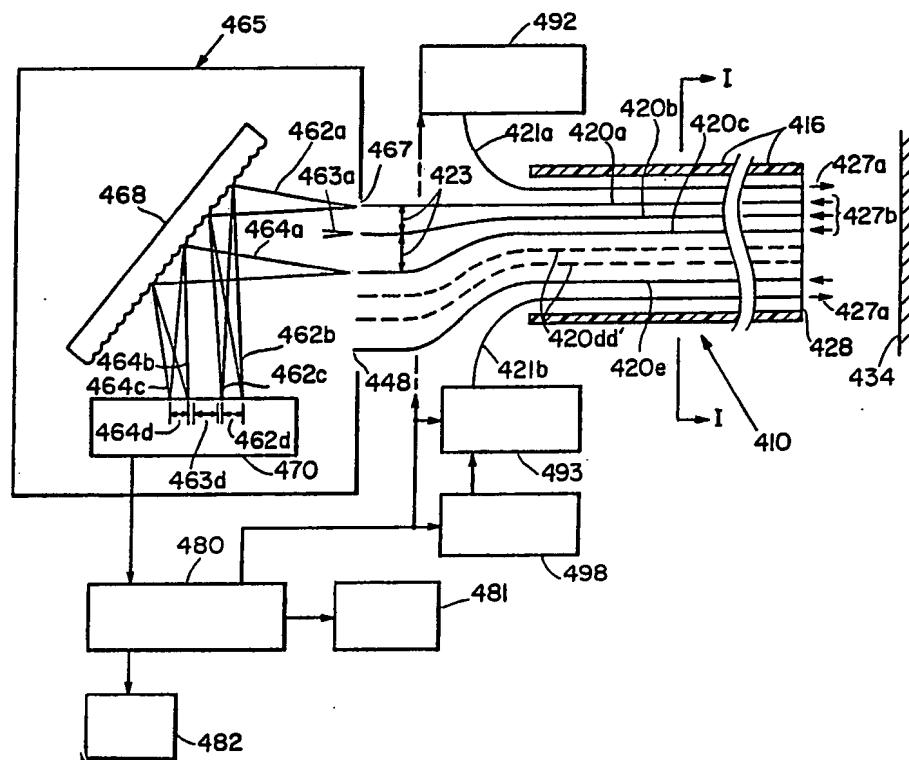
(57) Abstract

A catheter system for imaging wherein optical fibers within a catheter are used to illuminate tissue for diagnostic purposes. Both spectroscopic and visual displays of the tissue are generated simultaneously. Fluorescence and Raman

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CATHETER SYSTEM FOR IMAGING

Technical Field

This invention relates to devices in which optical fibers are provided within a catheter which is coupled to a spectrometer with an imaging detector and

05 diagnostic light is used to create a spectral image of the target tissue.

Background of the Invention

Optical spectroscopy is proving to be a powerful tool for probing the type and condition of tissue.

10 Images of tissue may be recorded remotely, and in vivo, using flexible coherent bundles of optical fibers. Spectra may be recorded in a conventional way using a scanning monochromator. But this is time consuming and inefficient in using the often weak

15 signals associated with tissue spectroscopy, especially where fluorescence excessive intensity may damage tissue thermally and excessive fluence may damage tissue photochemically or by other means. A spectrograph fitted with an imaging device, such as a

20 linear diode array, charge coupled device (CCD), charge injection device (CID), vidicon or other such imaging device, converts the entire dispersed spectrum into an electronic signal so that all the desired light is detected simultaneously. As the spectrograph

25 may be connected to an optical fiber, the emitted

spectrum is recorded. The other end of the fiber may be placed in tissue or at the bottom of a well or in other remote locations, to collect the light carrying information about its environment. However, this

05 device records only a spectrum, not an image. Similarly, coherent bundles of optical fibers transmit images from remote locations, which are recorded on similar electronic imaging devices for video display and storage. However, combining spectral analysis and

10 imaging has proved more difficult.

There is a need for a means to spectrally record the entire image simultaneously. Instead of using a single optical fiber consider the use of an image from a coherent bundle of optical fibers that is placed at

15 the entrance of a spectrometer. If the image was monochromatic, then a monochromatic image would also form on the imaging detector at a certain location, depending on the position of the grating, or other dispersing device. A spectrograph with an adequate

20 flatness of field is assumed here. If a second color was added to the image, then a second image would form on the detector, displaced from the first image, but in some part overlapping the first, depending on the amount of dispersion. Any given detector element

25 might be detecting light from one part of the image of one color, or another part of the image, of a different color. The output would be ambiguous. As more colors are added to the input image, a single element would detect more and more different parts of

30 the image in different colors, with no intrinsic way to sort out the mixed data. The imaging detector will

obtain a quite unsuitable spectrally blurred or
smeared image.

Fluorescence and laser induced fluorescence has
been used to diagnose tissue type and condition. A
05 wavelength of 480 nm excited fluorescence in the range
of 500-650 nm has been used, whereby the ratios of
peak and valley signals were useful to distinguish
atheromateous plaque from normal artery wall. In
Alfano, visible laser excitation induced fluorescence
10 in cancerous and normal tissue, with emission over a
range of 500-700 nm, which showed differences in the
spectra for the tissues. However, other wavelengths
of excitation and detection may be useful. Fluores-
cence emission characteristics of a particular chromo-
15 phore tend to occur at the same wavelength, for a
broad range of excitation wavelengths.

A different type of spectroscopy, termed Raman
spectroscopy, depends on a frequency shift from the
exciting laser line. The Raman spectral peaks will
20 occur at a fixed frequency separation from the laser
line, and, in principle, occur for any excitation
wavelength. It is the frequency difference that is
the most distinguishing feature. Raman spectroscopy
has been used for identifying a wide range of sub-
25 stances such as molecules in solution or in flames.

Summary of the Invention
In accordance with the invention, the optical
fibers, the spectrometer, and the detector will be
configured in a novel way so that information adequate
30 to construct both image and spectra will be obtained.

consider a specific embodiment and number of optical
fibers described below; but the invention need not be
limited in this manner.   A coherent optical fiber
bundle comprised of 10,000 fibers in a square array,
05 having 100 columns of fibers side by side, with each
column containing 100 individual fibers in vertical
array. Each fiber has a 10 micrometer core and a 20um
outer diameter, including cladding. The coherent
bundle forms a square with a 2mm cross section at the
10 input or distal end. At the output end, the columns
are separated one from another and spaced to a
distance of 500um to form a rectangular array 2mm by
50mm. This array, or an image of the array is placed
at the entrance of low-dispersion spectrometer which
15 is corrected to have adequate flatness of field and
minimize other abberations. For no magnification, the
dispersion is chosen so that the spectral region of
interest does not exceed 500um. This spectral region
may be limited with filters to avoid overlap.
20 Dispersion in the horizontal plane will be assumed
throughout this description, but it need not be
limited to this plane. Impinging on a 2-dimensional
image detector of adequate dimension (at least 50mm
wide in this case), is such that the dispersed spec-
25 trum of each column will not overlay that of the next
column. For a detector with a 20um square element,
each pixel element, corresponding to each optical
fiber, will be dispersed over 25 detector elements,
subdividing the spectrum into 25 resolution elements.
30 Thus, each of the 10,000 optical fibers will couple to
a separate 25 elements of the detector which has

250,000 elements, so that each spectrum may be
recorded individually without overlapping another
spectrum.

For a more compact system with a square detector
05 array, columns of fibers could be placed one below
another in groups. For example, if 5 columns from the
coherent bundle were combined into a single column
500 fibers each 10mm long, and there were 20 such
columns spaced 500um apart, this would form a square
10 array 10x10mm and could be projected onto a square
detector with or without magnification. Without
magnification each image pixel would be dispersed over
25 detector elements. A larger number of detector
elements, and appropriate adjustments of column
15 spacing and magnification would allow for more
spectral resolution elements per pixel.

Another arrangement of optical fibers would
consist of subdividing the square array into a square
block rather than columns. For example, a 5x5 block
20 of fibers could be relocated, and arranged into a 25
fiber column. The image would be dispersed onto a
square portion of the detector 25 elements high by 25
elements wide. The adjacent block of optical fibers
would be imaged onto a corresponding adjacent block of
25 the detector. This would minimize crosstalk problems
between widely separated parts of the image, as adja-
cent parts of the image are observed by adjacent parts
of the detector. With this type of arrangement, a
lower resolution image could be obtained if desired.
30 The block of optical fibers and corresponding block on
the detector might be treated as a single pixel. Of

course, any arrangement of optical fibers of the distal end might be matched in many ways to the image detector. For example, a single linear array could be used for a small number of optical fibers.

05   Special optical coupling elements may be installed between the output of the optical fiber bundle and the spectrometer detector. Anamorphic elements, such as cylindrical lenses or prisms, can expand the image more in one dimension than another.

10 The rectangular 2mm x 50mm image previously described could be changed to a rectangle of different dimensions, or even a square. Likewise, the round image of a single optical fiber can be made oblong to match a rectangular element on a detector array.

15   Optical fibers are not essential to this concept, however the image may be subdivided by small mirrors or beamsplitters to fall on different parts of the detector.

     An image may also be spectrally resolved with a
20 somewhat different type of apparatus. The image from the optical fibers is collimated and sent through a travelling Michelson interferometer. A single pixel undergoes constructive and destructive interference as the travelling mirror moves; the recorded spectrum as
25 a function of time is converted by Fourier transform to a wavelength spectrum. If however, the detector is replaced by an imaging device, such as a CCD, then every pixel is subject to the interferometer. The imaging device needs to be "read out" many times as
30 the mirror scans, so as to provide enough data for an accurate transform to be obtained. As an example, the

CCD would be read out entirely twenty times for each wavelength of travel of the mirror. The time to acquire a spectral image may become significant. Also, substantial computing power should be needed to do the Fourier transform of the data for thousands of pixels in a small amount of time.

Another system which can spectrally filter an image from an optical fiber bundle would be comprised of filters and beamsplitters. The light from the image may pass through a series of beam splitters to fall on one or more imaging detectors. Dichroic beamsplitters will separate the light into various colors with minimal losses. Absorbing filters may also be interposed in the light path to select wavelengths, however these are less efficient. Multiple images, each of a different color, may impinge on a single imaging detector.

It is anticipated that there will be a broad range of uses for this type of spectroscopic imaging device, both within and outside of the medical field.

We have found ultraviolet excited laser induced fluorescence provides a useful diagnostic for arterial tissue distinguishing normal from plaque. Experiments used wavelengths from 220 nm to 330 nm for excitation, with detection ranging from close to the laser wavelength to 750 nm. Several useful laser induced fluorescence diagnostics were found. Two peaks and a valley in the range of 370-470nm are useful for distinguishing normal and plaqued artery. Even after laser ablation damage, the valley of about 420 nm persists. It is likely due to the Soret band of

porphyrin, probably from heme. These features should
also be useful for identifying other types of tissue
as well. Weak LIF emission also occurred in the range
600-700 nm with a peak at 650 nm, for the wide range
05   of ultraviolet excitation. Also, ultraviolet wave-
lengths shorter than 320 nm excite a broad fluor-
escence probably due to tryptophan, which for 220-280
nm excitation ranges form 290-380 nm with a maximum of
about 335 nm. The intensity, and the fluorescence
10   lifetime (typically about 3 nsec) varies with tissue
type and may provide a useful diagnostic.

A Raman peak useful for diagnostic occurs at
about $3300cm^{-1} \pm 150cm^{-1}$. Although excitation wave-
lengths in the range 220-228 nm were used, Raman
15   scattering occurs for all excitation wavelengths; it
is the frequency shift that is the distinguishing
characteristic. Plaque showed a much stronger Raman
signal than did the healthy arterial media. The
frequency shift remained relatively constant as the
20   excitation frequency was changed, proving that the
spectrum is a Raman process, and not LIF. This signal
persisted after laser albation damage, and was useful
in determining that when plaque layer was penetrated,
the underlying healthy media gave a weaker signal.
25   This change in Raman signal strength could be used as
a feedback control diagnostic to signal that plaque
has been removed, and that tissue ablation may be
halted.

Brief Description of the Drawings

Figure 1 is a broken longitudinal cross-section of the imaging catheter, spectrometer and a block diagram of the computer and outputs, illustrating a

05 preferred embodiment of the invention.

Figure 2 is a cross-sectional view of the imaging catheter.

Figure 3 is an optical schematic illustrating target illumination by the same optical fibers used to

10 collect the emitted or reflected light, and illustrates optical imaging of the proximal end of the catheter onto the spectrometer aperture.

Figure 4 is an optical schematic showing the use of dual detection systems.

15 Figure 5 is an optical schematic showing the use of a Michaelson interferometer.

Figure 6 is an optical schematic illustrating the use of a lens to image the target onto the distal end of the catheter.

20 Figure 7 shows fluorescence of a normal aorta artery wall stimulated by 329nm excitation. The left hand scale (ordinate) is intensity of fluorescence signal (figures 7-10 use the same conditions).

Figure 8 shows plaque fluorescence under the same

25 conditions of Fig. 7. This is a soft plaque, mainly fiberous and fatty. The peaks have shifted slightly in wavelength and in the height ratio; but the valley is much less deep.

Figure 9 shows the spectrum whereby an argon ion

30 laser, using multiple shots, has ablated through the

1-2mm plaque layer to reach the normal media beneath. Total dosage was about 5-10J/mm^2. The spectrum of the tissue at the bottom of the crater is shown. The spectral shape is somewhat altered, but a valley at about 425nm persists.

Figure 10 shows an adjacent region ablated by the argon ion laser, fewer exposures were made so the plaque was not penetrated. This spectrum is clearly distinguishable from Figure 9, showing that this is a useful diagnostic for determining when the plaque layer has been penetrated.

Figure 11 shows fluorescence from normal aorta using 320nm excitation.

Figure 12 shows fluorescence from plaque under the same conditions. This shows that useful diagnostic information can be obtained for various excitation wavelengths.

Figure 13 shows normal artery excited by 220nm, yielding a fluorescence peak of about 330nm, most likely due to tryptophan. A fluorescence lifetime of about 3nsec was observed; this may also yield useful diagnostic information.

Figure 14 shows plaque on the same artery sample, under the same conditions. As for Figure 13, the peak has less intensity. Any UV wavelength shorter than 330nm excites this fluorescence.

Figure 15 using 280nm excitation, a weak peak at 650nm is seen. The detection sensitivity is high so the tryptophan peak is off scale. This is for plaque.

Figure 16 shows a fluorescence spectrum for normal tissue, under the same conditions as for Figure 15 showing greater intensity for the 650nm peak.

Figure 17 shows a Raman peak at about 244nm. The laser line is about 225nm. (A correction of -2nm is needed for all following Figures 17-22). There is an intensity scale change at about 233nm. This spectrum is for soft plaque, fiberous and fatty. The frequency shift is about $3,320cm^{-1}$. This corresponds to an O-H stretching frequency, or possibly that of N-H.

Figure 18 shows a spectrum for normal arterial media on the same tissue sample. The Raman peak is much weaker.

Figure 19 shows a spectrum of calcified plaque which has been irradiatedwith about 2 Joules/mm^2 from an argon ion laser, 514nm. The strong Raman peak at 244nm is present, with a frequency shift of $3,320cm^{-1}$.

Figure 20 shows a different excitation wavelength for one laser 222nm; the Raman peak has moved also proving that this is Raman and not fluorescence emission. The difference in frequency is about $3,290cm^{-1}$, which is unchanged within experimental error..

Figure 21 shows a Raman spectrum of plaqued aorta artery wall whereby the plaque has been ablated away as described for Figure 9. The Raman peak at about 242nm is weak, indicating that the overlying plaque has been removed.

Figure 22 shows Raman spectrum of ablated plaque which was not penetrated, similar to that described for Figure 10. The Raman peak at about 242nm is

strong, indicating that there is still plaque at the bottom of the crater. A weak "shoulder" peak is seen at about 232nm corresponding to about a 1600cm^{-1} Raman shift which could be a carbonyl stretching frequency;
05 this may also have useful diagnostic properties, but better laser light rejection will be needed to examine it.

Detailed Description of the Invention

Figure 1 shows a preferred embodiment of the
10 invention. The catheter 410 is shown in broken longitudinal section. It has a distal end 428 and a proximal end 448 and contains 10,000 imaging optical fibers or similar light conduits in a 100 by 100 square array. Optical fibers 420 a,b,c,e are shown, with 420
15 dd' indicating the large number of additional optical fibers in the array. Illuminating optical fibers 421 a,b are coupled to a laser source 492 or a conventional light source 498 with wavelength selection 493 comprised of filters, a monochromator,
20 or similar device. Illuminating light 427 a emergers from illuminating fibers 421 a,b and falls on the target tissue or sample 434, which may or may not be in contact with the catheter. Light returning 427 b from the sample is collected by the fibers 420 a-e to
25 be delivered to the spectrometer 465.

Since this is a cross-sectional view, each optical fiber illustrated actually represents a column of 100 optical fibers. These columns of fibers are physically separated by a distance indicated by arrow
30 423 at the proximal end 448 of the catheter and all

are placed at the entrance aperture 467 of the spectrometer 465. The emitted rays of light from each column of fibers 420 a-e fall on the grating 468 and are dispersed. The grating may be self focussing as shown, or the spectrometer 465 may contain additional optics to produce the image at the two dimensional detector array 470. Because of the physical separation 423 between fibers, the spectrally dispersed images 462d, 463d, and 464d of the fibers will be physically separated on the detector array 470. Light rays 462a spreading from fiber 420a are dispersed in the horizontal plane with the longer wavelength rays 462c and shorter wavelength rays 462b impinging on the detector 470 over a range of 462d. Similarly, rays 464a from fiber 420c are dispersed to long 463d. These spectral ranges do not overlap, so that spectra are recorded separately.

From detector 470, the electronic signals go to the computer and controller 480, where they are processed and displayed as a spectral map on terminal 482 or output as hard copy on 481. The computer may also control light source 498, scannable monochromator or changeable filter wavelength selector 493, or laser light source 492. Both excitation and emission spectra may be obtained. The computer 480 records the spectrum from each optical fiber to construct the spectrum from each optical fiber to construct the spectral image; the light from each fiber 420 a-e represents a pixel of data for the image. With suitable algorithms, the spectra are compared to stored spectra and converted to diagnostic information

about each pixel, such as tissue type, and presence or
absence of disease. An image showing such a condition
is displayed on the monitor 482, or printed out on
481.

05   Figure 2 shows a cross section of the optical
fiber catheter 410 in a preferred embodiment, with the
array at 100 columns of fibers containing one hundred
fibers each. The first column comprises the fibers
520a, 521a, 522a, 524a, and with more fibers indicated

10 by dotted line 523a. The second column has fiber 520b
at the top, and the third column has fiber 520c, the
last column has fiber 520e at the top. Additional
columns are indicated by dotted lines 520 d-d'.
Illumination fibers 421 are shown at the periphery,

15 although they may also be located between the columns.
An optional inner sleeve surrounds the fibers. The
whole is contained in an outer tube or catheter 416.

Figure 3 is an alternate embodiment where by the
proximal end 448 of the catheter is imaged onto the

20 aperature 467 of the spectrometer 465. Lenses 541 and
542 make, the image, but mirrors or other optics may
also be used for the purpose. Rays 564a from the
optical fibers are collimated 564b and focussed 564c.
Optional beamsplitter 552, which may be dichroic or

25 partially reflecting, .allows illuminating light 594a
from source 592 and coupling selector 546 to be
coupled directly into the optical fiber bundle 520.
The rays 594b are focus 594c onto the proximal end of
the catheter 448. Selector 546 may contain optics and

30 beam directions to allow coupling into any or all of
the optical fibers 420 a-e in the catheter 410.

Figure 4 shows an alternate embodiment using two spectrometers. The light emerges from the proximal end 548 of the catheter 410. The columns of fibers in the bundle 520 need not be separated. Rays 564a are
05 collimated 564b by lens 541a and are divided by partially reflecting beamsplitter 552a. Some of the light rays 564c form an image on the aperature 467a of spectrometer 465a. Some of the 564d pass through image rotating prism 549 or similar optical system.
10 The rays 564e now rotated through an angle such as 90°, reflect from optional mirror 548 and are converged 546f by lens 543a to form an image on aperature 467b of spectrometer 465b. As in Figure 1, the two spectrometer detectors are connected to a
15 computer where the data from the two spectrally dispersed images can be processed.

Figure 5 shows an alternate embodiment using a Michaelson interferometer. The proximal end 548 of the optical fiber bundle 520 has light rays 564a which
20 are collimated by lens 541b, entering into Michaelson-type interferometer comprised of beam splitter 552b, fixed mirror 545 and movable mirror 546. The exiting lights is focussed by lens 542b, and the rays 564g are imaged onto two dimensional detector
25 570. The computer 580 is capable of performing Fourier transforms of the data from all of the elements on the detector. The detector 570 need have only as many elements as there are optical fibers in the bundle 520, since this is a non-dispersive system.
30 Figure 6 shows an alternative embodiment with collection optics at the distal end of the catheter.

Lens 441 collects light rays 560a eminating from
tissue 434 and focusses the rays 460b onto the distal
surface 428 of the catheter 410, for illustration, the
rays corresponding to optical fiber 420c are shown.
05 An optional optical shield 412 may be used to protect
the optics.

In alternate embodiments, any number of optical
fibers may be arrayed in the catheter in a square,
hexagonal, circular, or other patterns. In Figure 4,
10 the beam is divided into two components to be directed
into two spectrometers. Additional beamsplitters or
mirrors may be used to further subdivide the beam
before going to the spectrometers. Other coupling
optics, represented by those in Figure 3, may be used
15 to magnify the image or expand it anamorphically to
better suit the shape of the detector. Columns of
optical fibers may be combined or separated so that
the number of columns at the proximal surface is not
the same as the number in the catheter, and the number
20 of fibers within a column may also be changed. This
will better match the geometry of the fiber array to
that of the detector. More than one detector array
may be used to obtain adequate coverage of the dis-
persed spectral image. This device may be used for
25 medical imaging on any application where it its
desirable to obtain both spectral and spatial imaging.

Whole arterial wall was placed in a capped fused
silica cuvette, flush against the face, with moist
clean paper behind the tissue to prevent drying.
30 Pulsed ultraviolet laser light was used to excite
fluorescence in the tissue. The fluorescence was

collected with fused silica optics and passed through a scanning double monochromator onto a photomultiplier. After gated integration, the signal was stored in a computer.

05   Excitation with about 329nm generated fluorescence from the laser wavelength to the sensitivity limit of the photomultiplier at about 700nm. Peaks were observed at about 395 and 450nm ± 10nm with a valley at 425 nm. The valley was deep for

10 normal artery wall and shallow for plaque. Ablation damage from high power exposure with an argon ion laser upon the tissue altered the spectra, making the valley shallower in both cases. But differences remained, showing that diagnostic difference persists

15 after laser damage. The valley is probably due to reabsorption by the Soret band of porphyrin, probably from heme. Shorter wavelength excitation using wavelengths as short as 220nm excited strong fluorescence at 335nm, most likely from tryptophan. A

20 fluorescence lifetime of a few nanoseconds was observed for this emission and for other emission wavelengths as long as 550nm. The intensity and time resolved fluorescence characteristics of these spectra should provide tissue diagnostic information. Weak

25 emission at 600-700nm, with a peak about 650nm, also appearing to be a useful diagnostic and occurs for all ultraviolet excitation.

For fluorescence spectroscopy, the molecular chromophone is put into an excited electronic state by

30 absorption of a photon of light. The emission is characteristic of the particular chromophone; the peak

wavelength tends to remain constant when the excitation wavelength is changed. But excitation wavelength must match the chromophone absorption band.

Raman spectroscopy, which probes the vibrational energy levels of a molecule, eliminates this problem as almost any wavelength can be used. Due to the vibrational transitions of molecules contained in the material under study, light incident upon the material is inelastically scattered thereby transferring energy to the molecule and typically causing a decrease in the frequency of the scattered light.

The use of Raman spectroscopy for diagnostic purposes in distinguishing artery wall from atheromateous plaque via an optical fiber bundle disposed in a catheter is claimed.

Excitation at shorter wavelengths, particularly around 220nm, yielded a Raman signal with about a 3300 ±150 wavemeter Stokes shift. This Raman signal was much stronger for plaque than for healthy artery wall. Since the shift is constant and independent of the excitation wavelength, it is a Raman signal. Such Raman signals should occur for all excitation wavelengths, although it is more difficult to observe when there is strong fluorescence emission also. The Raman signals persisted after the tissue was ablated with a high power argon ion laser. When the argon laser ablated an overlying layer of plaque, exposing normal media underneath, the Raman signal was substantially reduced, indicating that this signal is a useful diagnostic for determining when the plaque layer has been penetrated.

The Figures 17-22 show the data which illustrates
the use of the Raman diagnostic for distinguishing
plaque from underlying media. For the diagnostic to
be useful for monitoring an ablation process, spectral
05 differences should be present after ablation.
Although the spectra of normal arterial tissue change
to some extent after ablation has occurred, the plaque
and healthy media can still be distinguished. In
addition, the changes which occur as a result of
10 ablation can be useful as a tissue damage monitor.
Most important, however, is a means to determine when
the plaque has been penetrated, and that media has
been reached so that a signal can be generated to warn
the operator that the process should stop; or the
15 signal could be used as a feedback control to
terminate laser firing through the particular optical
fiber automatically.

Since the Raman scattering generally occurs from
a relatively simple functional group, in this case the
20 hydroxyl group (OH) or perhaps a nitrogen-hydrogen
(NH) bond, it is probably quite photochemically and
thermally stable, and resists laser damage. This is
unlike the case for laser induced fluorescence which
generally involves molecular chromophores and are more
25 likely to suffer such damage. This makes the Raman
spectra a promising new diagnostic tool for monitoring
a tissue ablation or treatment process.

Raman scattering occurs for many frequencies as
well. A signal is observed of about $1600cm^{-1}$, but is
30 partially obscured by scattered laser light passing

through the scanning monochromator. This frequency
shift may also prove to be a useful diagnostic.

In order to more accurately determine the fre-
quency shift, the monochromator was scanned over the
05 laser line, with the light-detecting photomultiplier
adjusted to low gain. About 5-8 nm past the laser
line (longer wavelength), the photomultiplier gain is
greatly increased, resulting in a sharp rise in the
signal on each Raman scan.
10   The following data taken from a number of scans
prove that the peak is a Raman peak, and is not due to
laser induced fluorescence.

Spectrum Number	Laser Wavelength cm^{-1}	Raman Shift cm^{-1}
1	43,971	3263
2	43,971	3298
3	43,191	3266
4	44,105	3197
5	44,165	3343
6	44,205	3228
7	44,245	3268
8	44,245	3177
9	44,420	3325
10	44,440	3314
11	44,440	3348
12	44,440	3365
13	44,504	3318
14	44,524	3167
15	44,524	3320
16	44,543	3323
17	44,823	3295
18	44,843	3263
19	44,843	3332
20	44,843	3366
21	44,863	3352

Even though the laser frequency ranges from 43,971cm^{-1} to 44,863cm^{-1}, for a difference of 892cm^{-1}, the spectral shift remains relatively constant and shows no pronounced trend, proving that the observed peak is a Raman peak, not a fluorescence peak.

CLAIMS

1. An optical system which is capable of generating
   a spectrally resolved spatial image of tissue,
   comprised of:

   05   a catheter containing a plurality of
   optical fibers forming a bundle;
               a laser coupled to the fibers to
   illuminate tissue with light;
               dispersion means for dispersing light
   10   emitted by the sample and carried along the
   bundle to said means;
               a detector array for receiving the
   dispersed light; and
               a computer for processing the received
   15   light such that the dispersed light is
   spectrally resolved and a displayable image
   of the illuminated tissue is formed.

2. The optical system of Claim 1 wherein the optical
   fibers are arranged within the catheter in a
   20   plurality of several separated columns such that
   the dispersed light exiting from one column does
   not overlap that from any other column on the
   array.

3. The optical system of Claim 1 wherein said
   25   dispersion means is comprised of:
               a self-focussing holographic grating.

4. A method of obtaining spectrally resolved spatial
    images comprising the steps of:

    placing the distal end of an optical
    multifiber catheter in contact with tissue
05 to be diagnosed;

    passing light through illuminating
    optical fibers onto the surface of said
    tissue;

    collecting light emitted from said
10 tissue and delivering it to an entrance
    aperture of a spectrometer with said optical
    fibers in separated columns, such that the
    dispersed spectra impinge on a detector
    array without overlapping; and

15 processing signals from said detector
    array in a computer to generate a spatial
    image of said tissue.

5. A method of diagnosis of the type of tissue in
    the artery, including distinguishing artery wall
20 from atheromateous plaque, comprising the steps
    of:

    providing a catheter with a plurality
    of optical fibers in which the distal end of
    the catheter is enclosed by an optical
25 shield having a fixed surface transparent to
    light radiation and spaced from the ends of
    said fibers wherein the proximal end of the
    catheter and optical fibers may be coupled
    to a source of optical radiation wherein the

radiation is capable of exciting
fluorescence and scattering light;

inserting said catheter into an artery
until the optical shield is brought into
05   contact with a suspected arterial lesion or
other tissue to be diagnosed;

selecting an optical fiber and coupling
said light at a wavelength from the light
source to the proximal end of said optical
10   fiber whereby the light enters the proximal
end of the optical fiber and is transmitted
by the selected optical fiber to the distal
end of said fiber out the optical shield and
impinges on the suspected lesion, and the
15   scattered light is returned to the proximal
end of the selected optical fiber, and is
coupled to a spectral analyzer wherein the
scattered light excited by said light is
analyzed to deterime if the material con-
20   tacted by the optical shield and, in
particular, the portion irradiated by the
incident light from the selected optical
fiber is healthy arterial tissue or plaque
or other material;
25   observing at the proximal end of the
selected fiber a Raman signal within the
scattered light excited by said light to
analyze the spectral profile where peaks
occur; and
30   determine from ratios of spectral peak
heights of the light and the Raman signal

whether the tissue being analyzed is artery
wall, plaque, blood or other tissue.

6.   The method of diagnosis of Claim 5 wherein the
light source is an argon ion laser.

05 7.   A method of diagnosis of the type of tissue in an
artery, including distinguishing artery wall from
atheromateous plaque, comprising the steps of:

inserting a catheter containing a
multiplicity of optical fibers into an

10   artery, said catheter and fibers having
proximal and distal ends with an optical
shield means on the distal end of the
catheter having an optically transparent
enclosure with a distal output surface

15   located a fixed distance from the distal
ends of the fibers and extending over the
end of the catheter and a distal surface for
displacing body fluid such that direct
contact can be made by said distal surface

20   with such tissue within the artery and a
laser source of light coupled to at least
one of said fibers at a proximal end;

terminating said insertion when the
optical shield is brought into contact with

25   a suspected arterial lesion or other tissue
to be diagnosed;

selecting an optical fiber coupled to
said laser source and coupling said light to
the proximal end of said optical fiber

whereby the light enters the proximal end of
the optical fiber and is transmitted by the
selected optical fiber to the distal end of
said fiber out the optical shield and
05   impinges on the suspected lesion to produce
fluorescence and associated fluorescent
light is returned to the proximal end of the
selected optical fiber, and is coupled to a
spectral analyzer wherein the fluorescent
10   light is analyzed to determine if the
material contacted by the optical shield
and, in particular, the portion irradiated
by the incident light from the selected
optical fiber is healthy arterial tissue or
15   plaque or other material, said analysis
including:
(i)   observing at the proximal end of the
selected fiber the fluorescence excited
by said light to analyze the spectral
20   profile in the range 360-500 nm, where
peaks occur; and
(ii) determining from ratios of fluorescence
peak heights at about 395 nm and 450 nm
and the valley at about 420 nm, whether
25   the tissue being analyzed is artery
wall, plaque, blood or other tissue.

8.   The method of Claim 7 wherein the laser light
source emits light at wavelengths in a range
between about 300 nm to 340 nm.

9.   The method of Claim 7 wherein less than 100
      microwatts of average power is used from said
      laser source to excite fluorescence.

10.   The method of Claim 7 including providing a beam
05   splitter near the proximal end of the catheter to
      allow use of the same optical fiber for both
      delivery of incident light from the laser and
      return of fluorescent light to the spectral
      analyzer.

Fig. 1

Fig. 2

Fig. 3

465a
542a 552a 541a
564c
564b 564a 420c
467a 564d 548 520 410

480

465b 549
564a
467b 564f Fig. 4
548a
543a

420c 412

460b 460a
410 428 441 434

545
546
552b 541b
564a
548 520

542b
564g
570 580 Fig. 5

Fig. 6

SUBSTITUTE SHEET
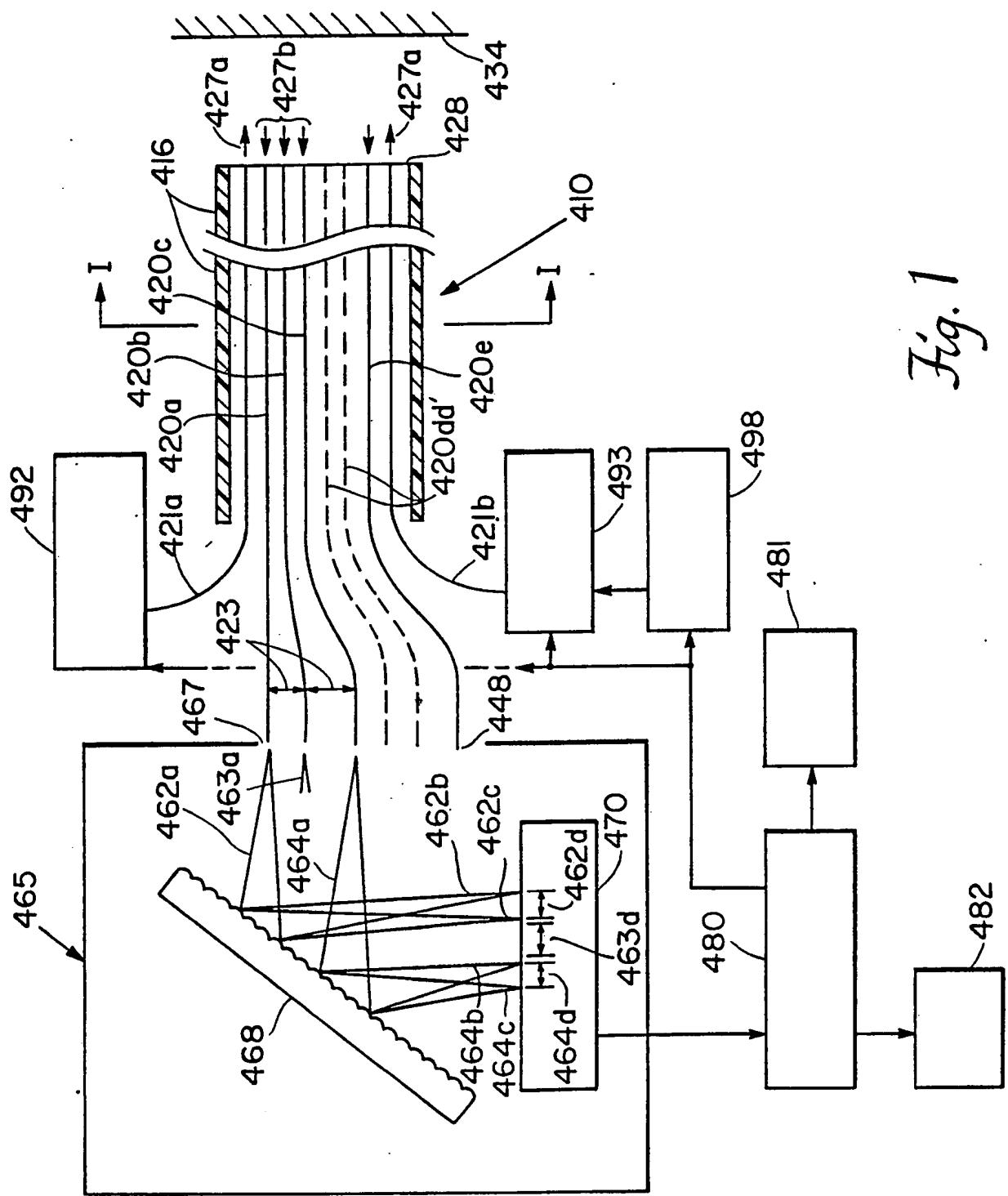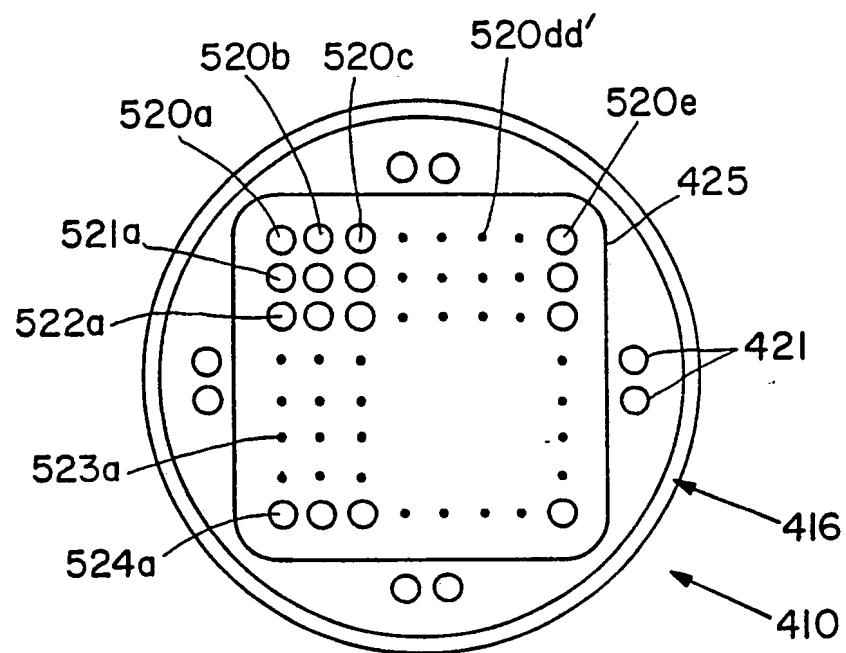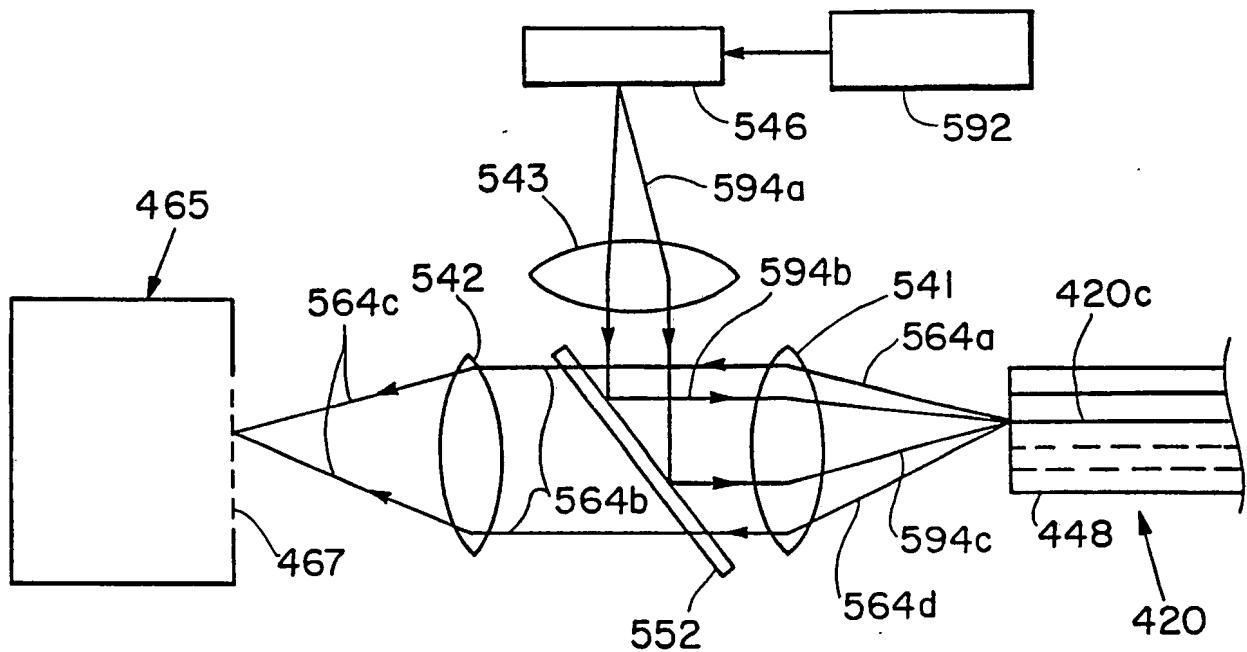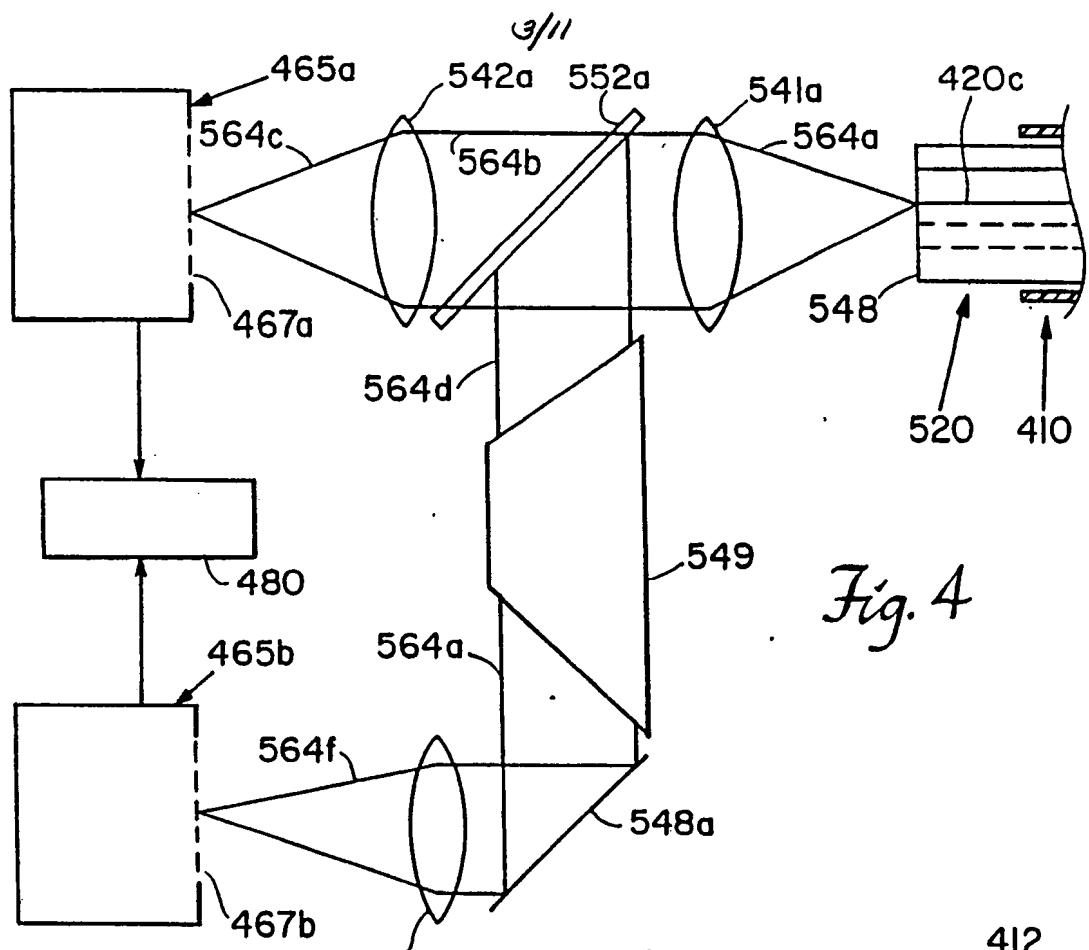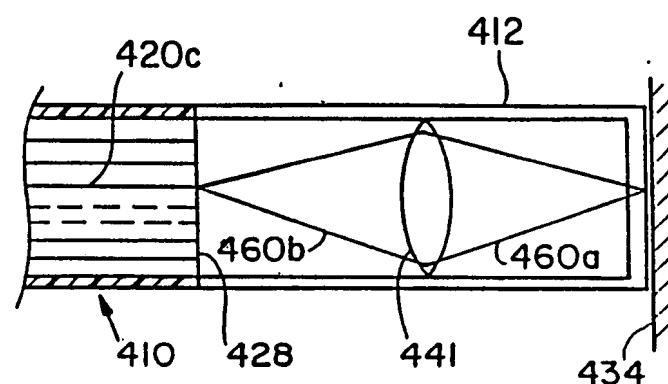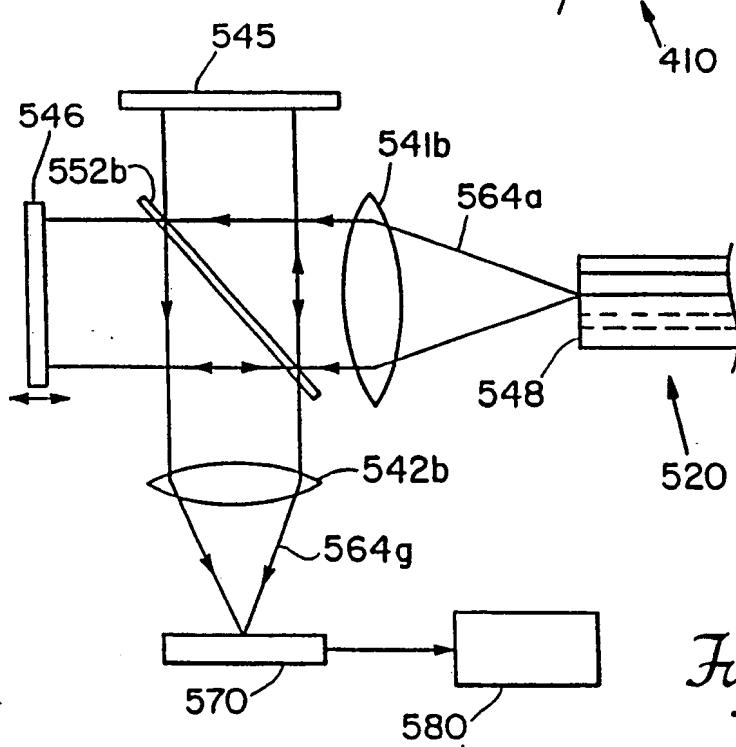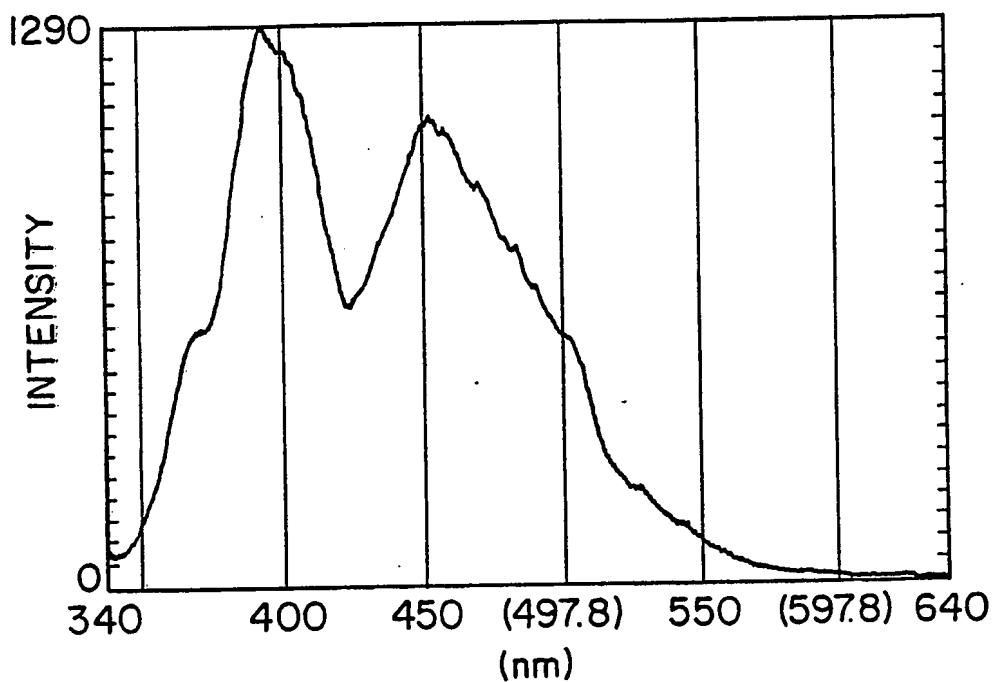
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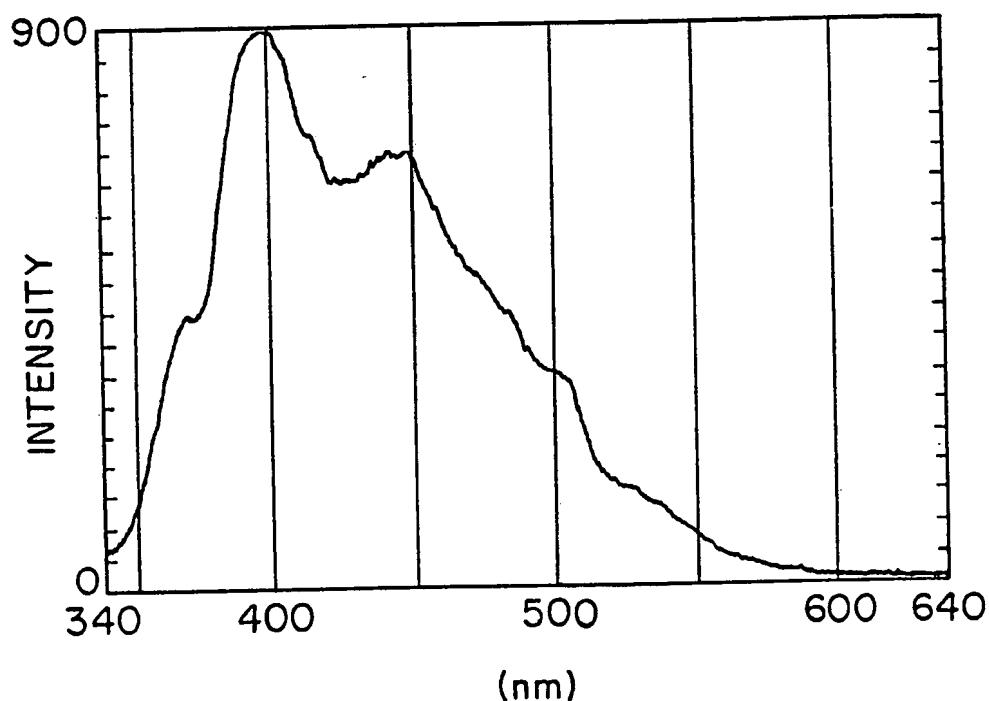
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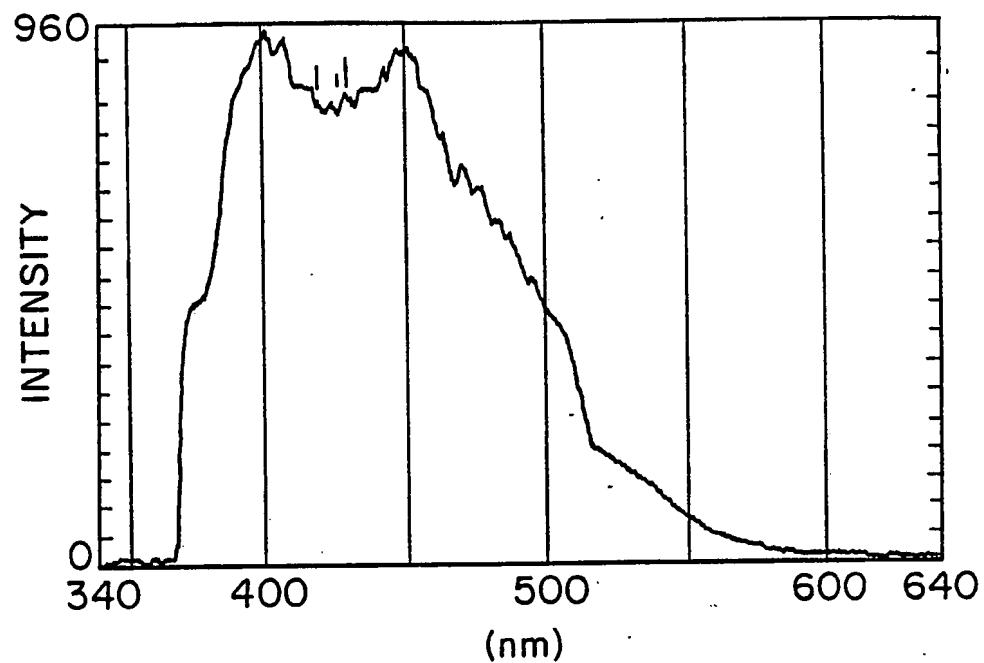
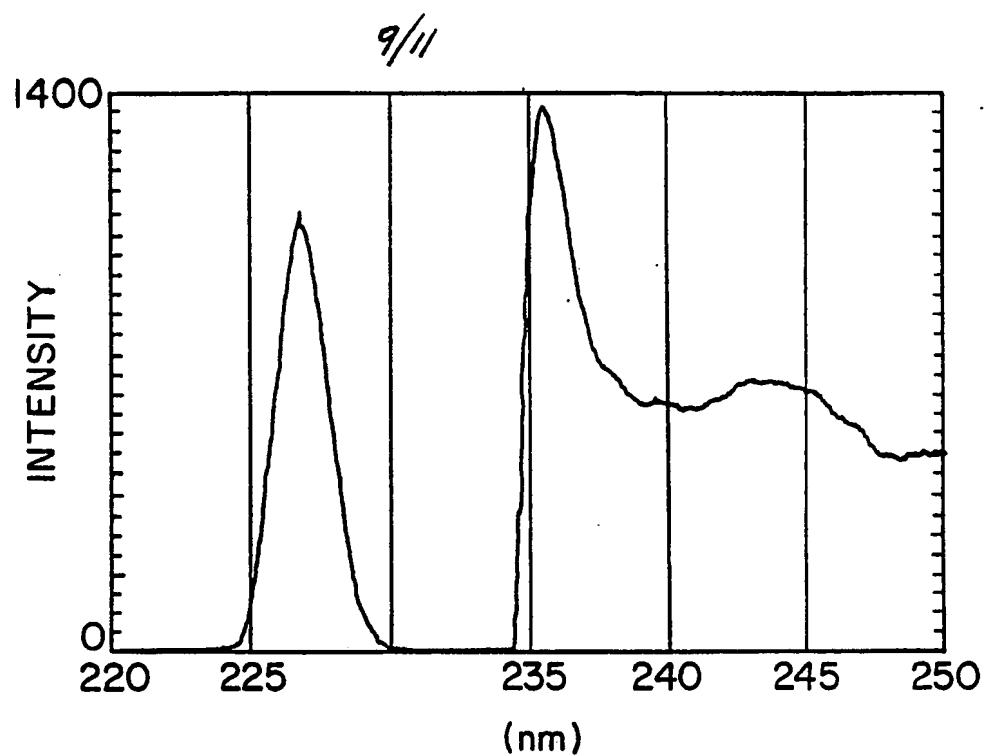*Fig. 9*
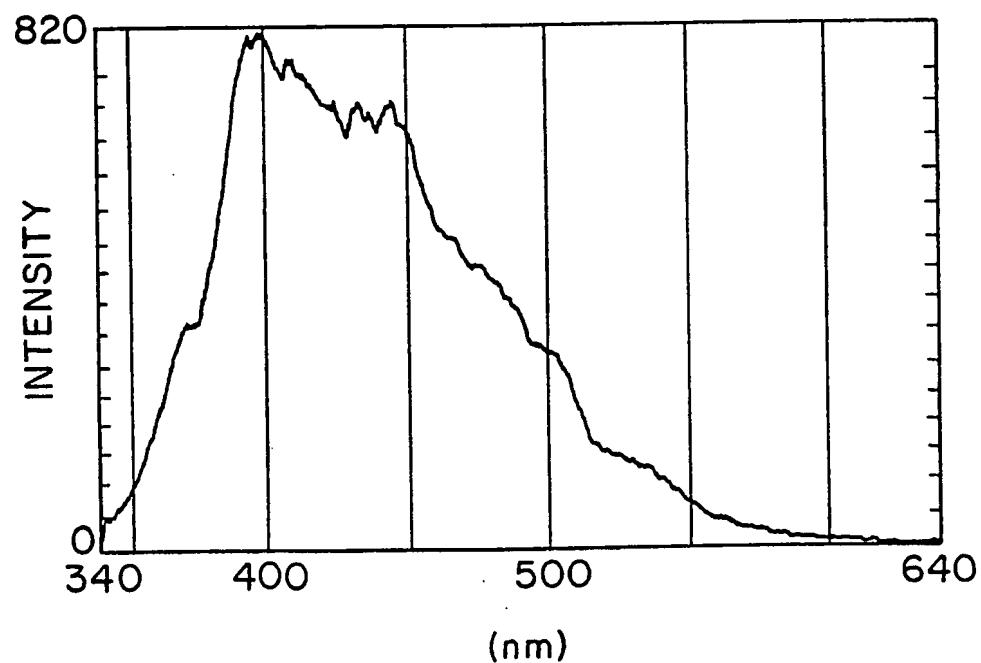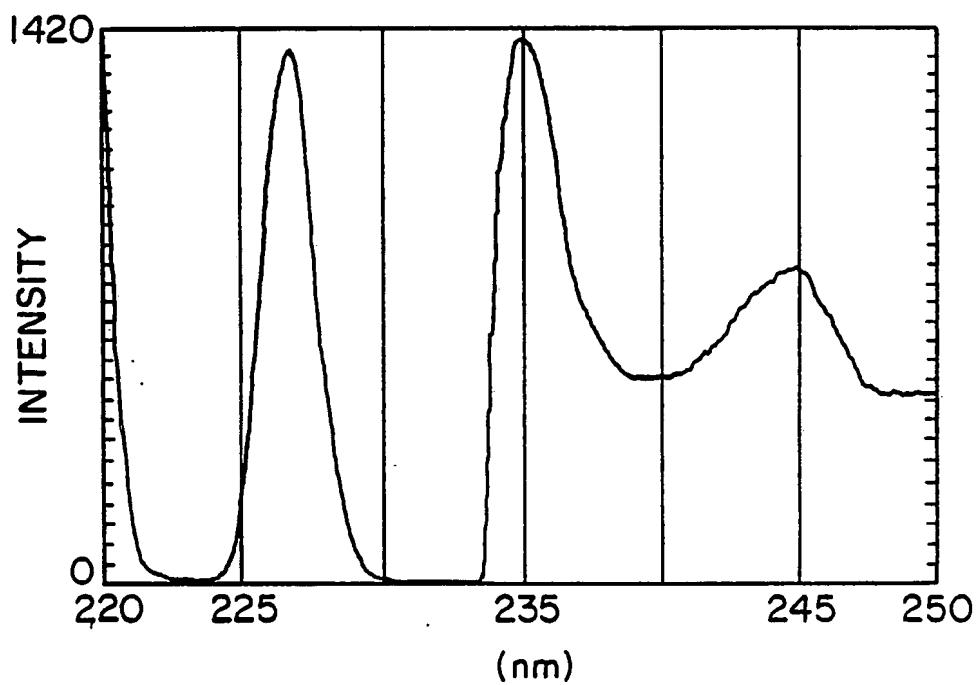

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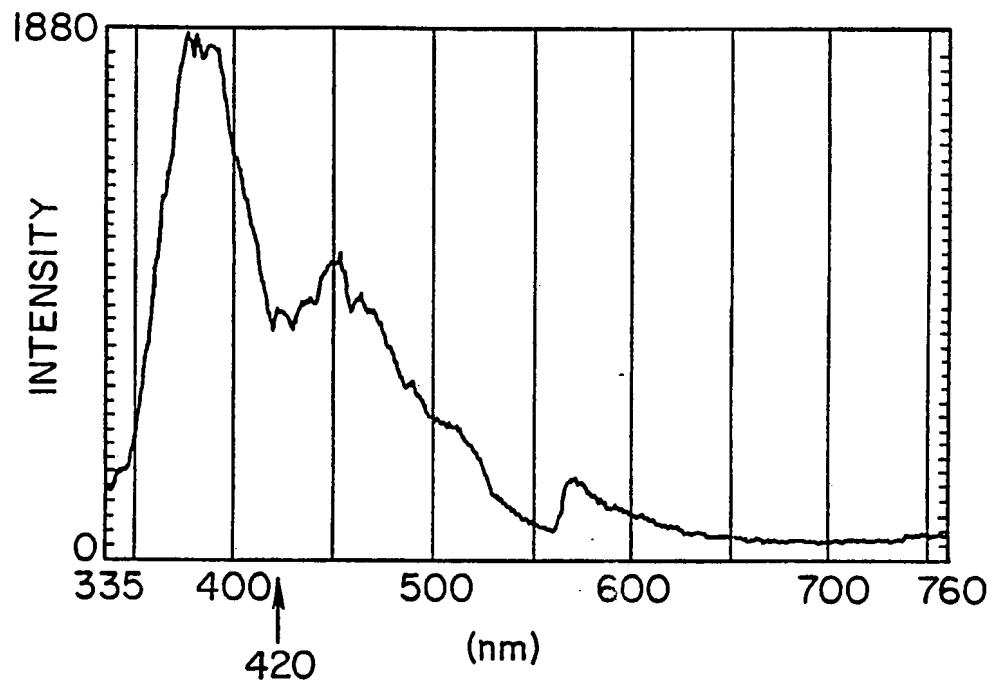
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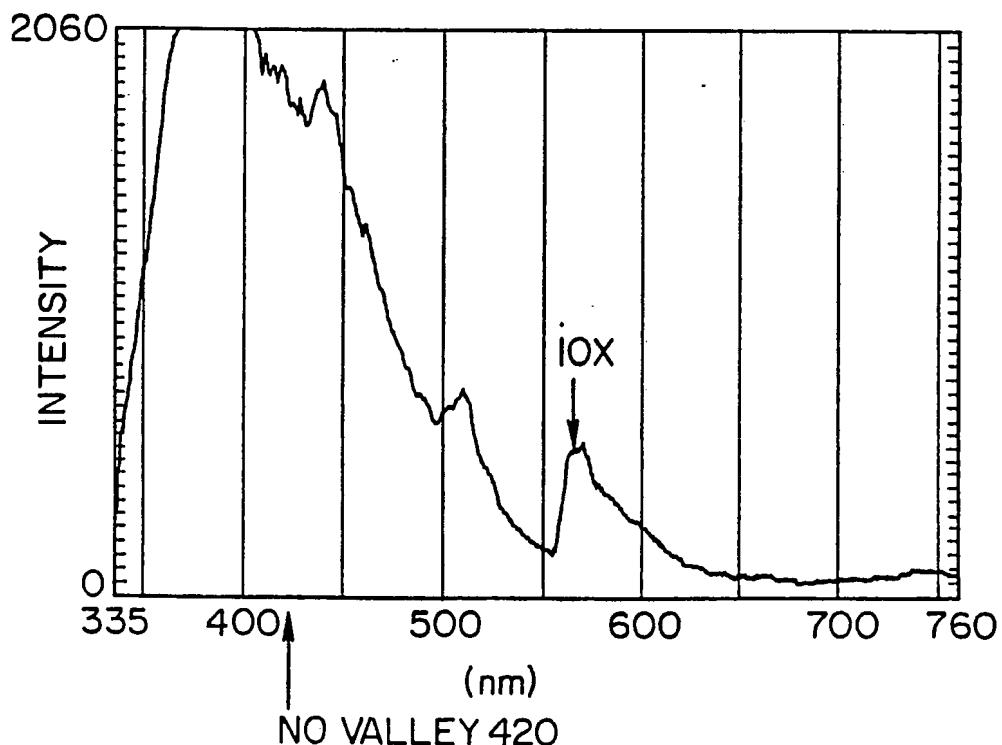
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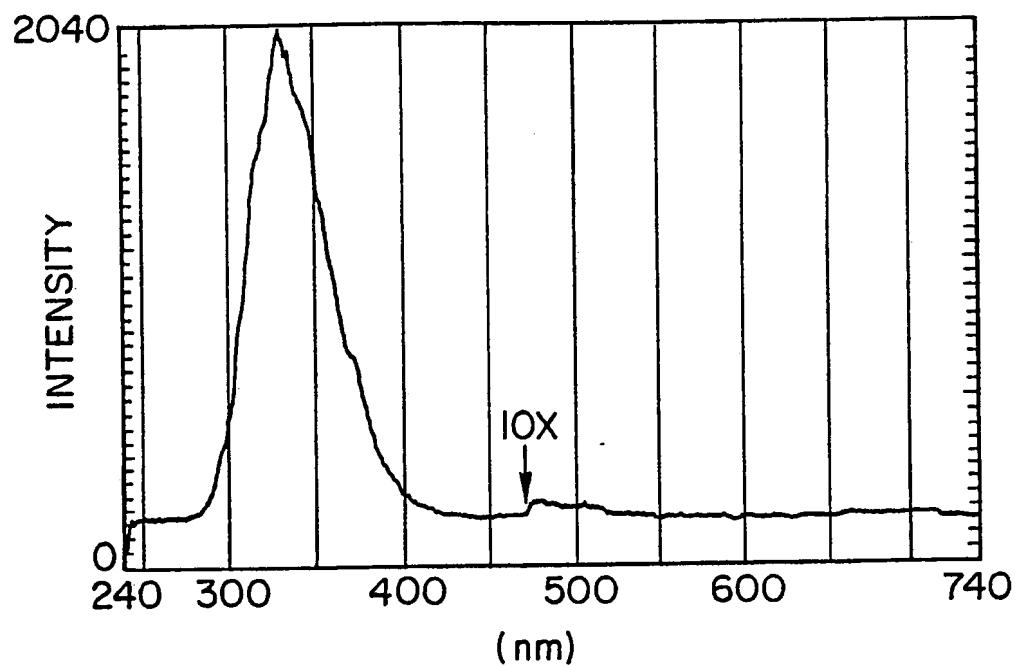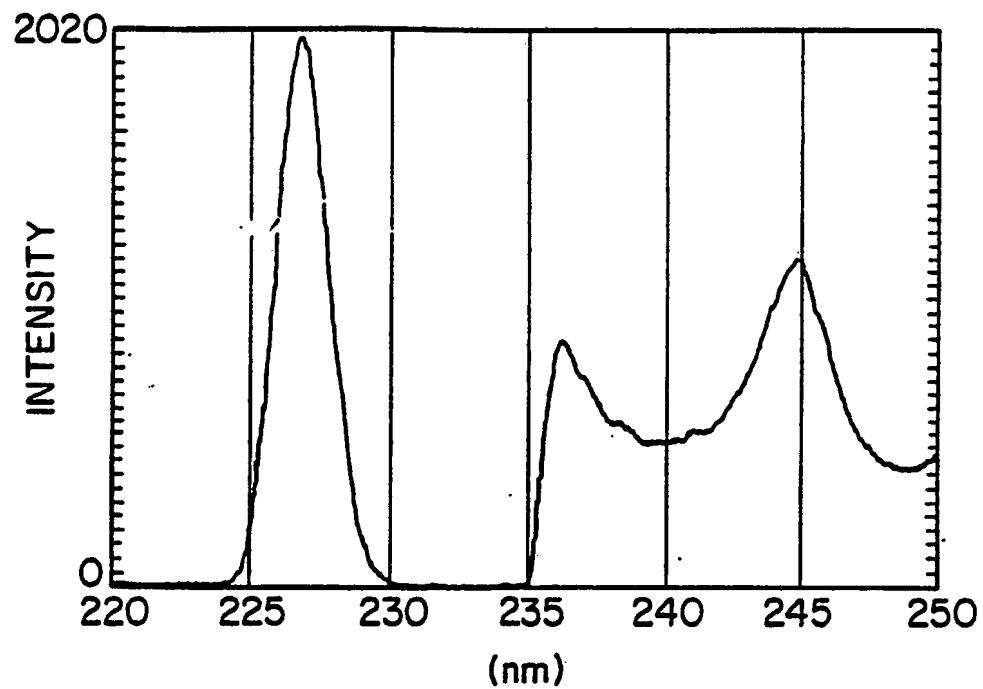
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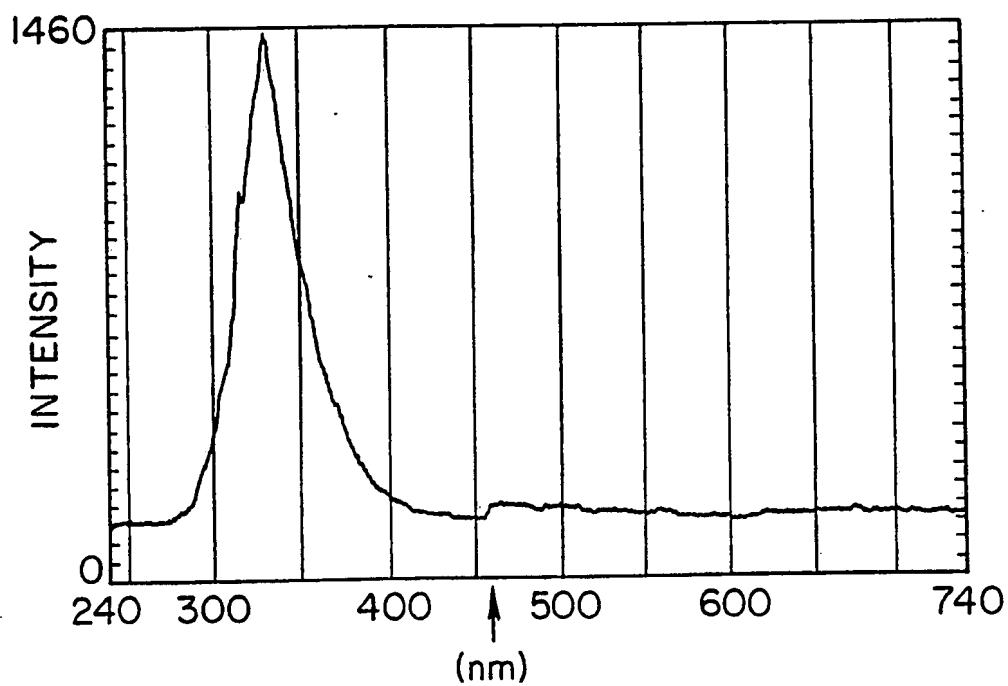
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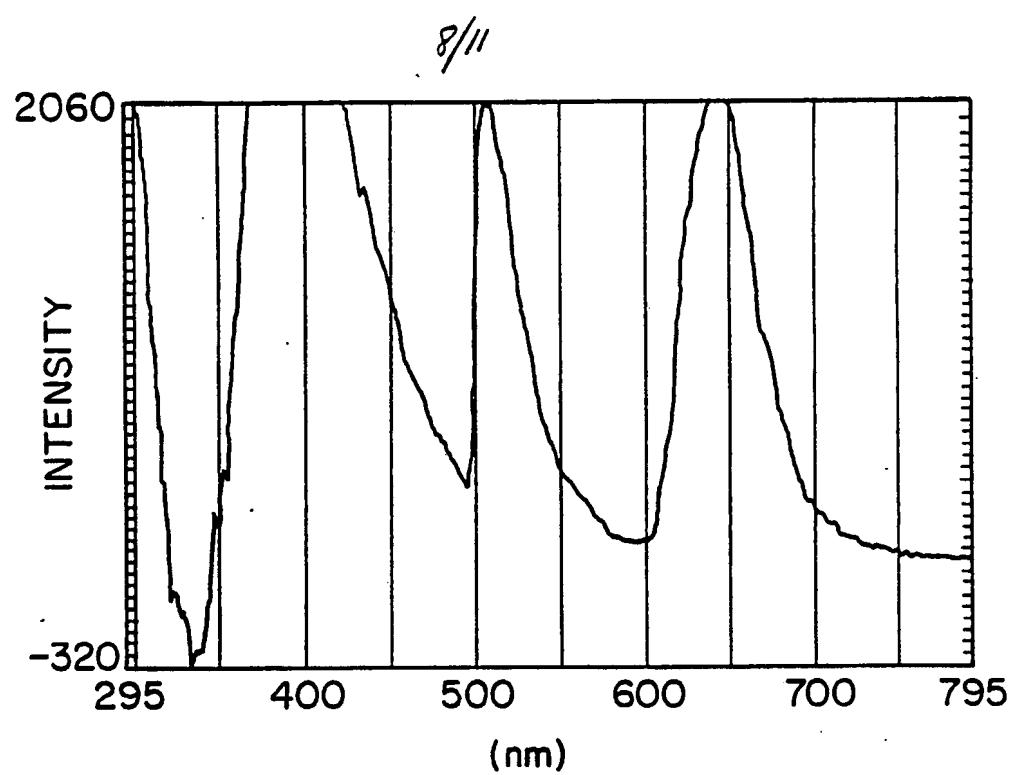
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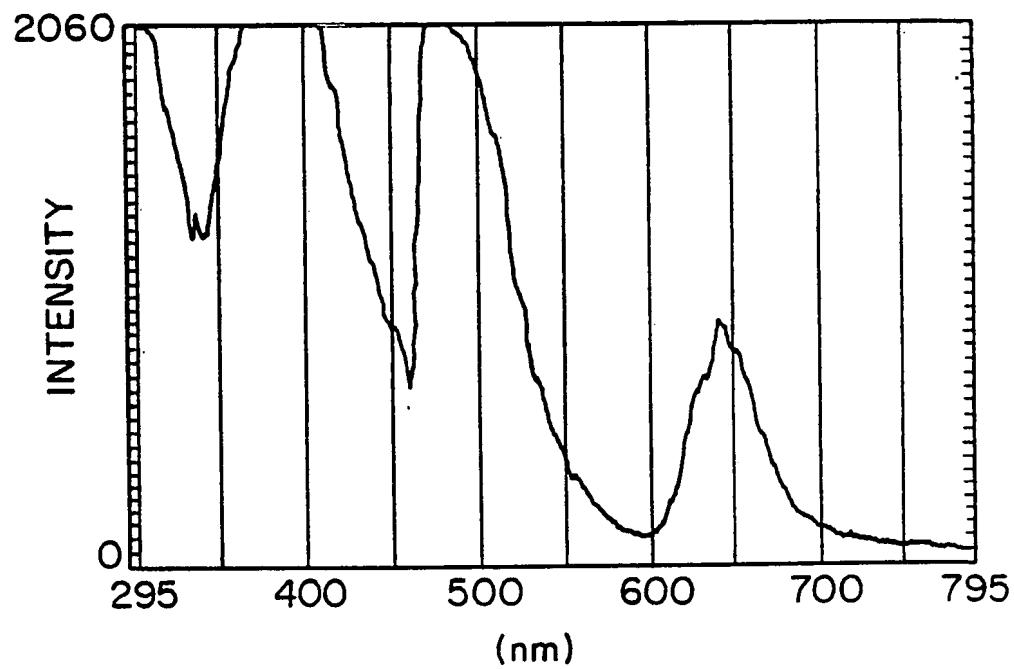
Fig. 15

Fig. 18

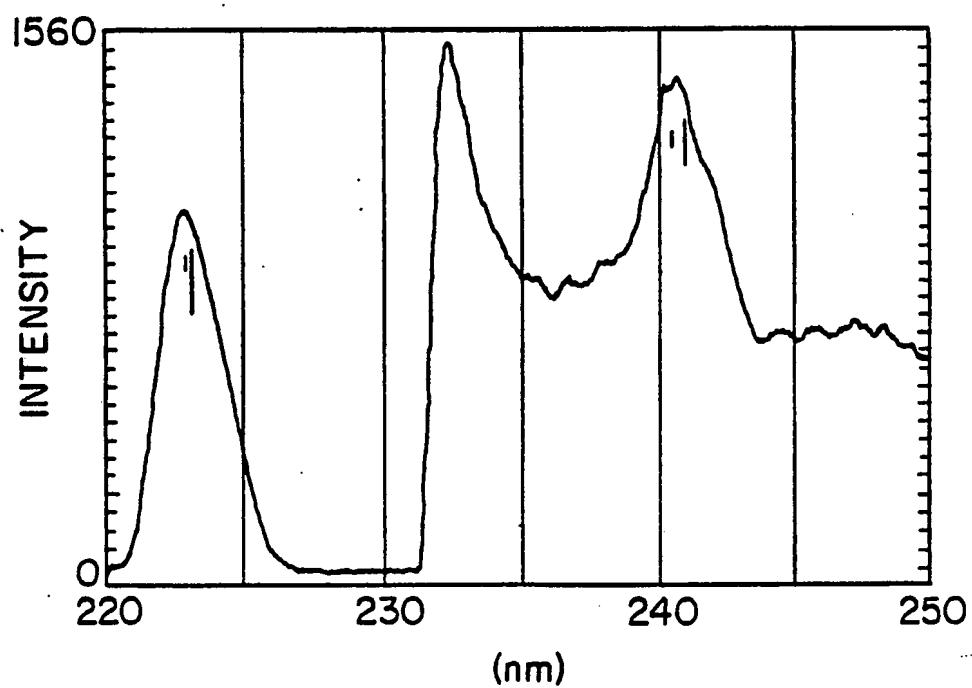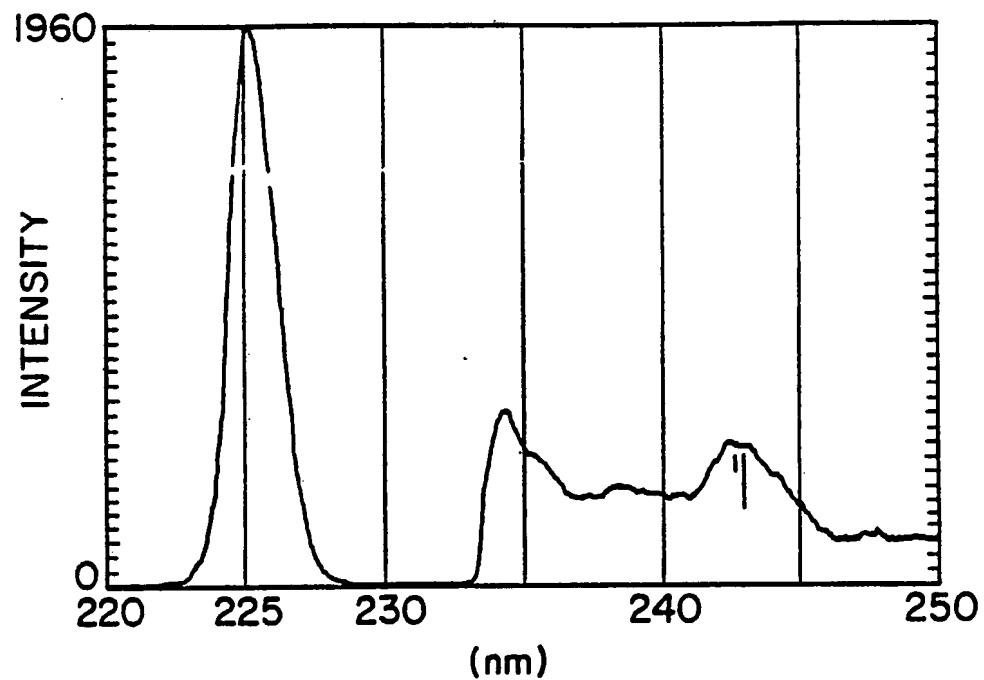*Fig. 17*

Fig. 19
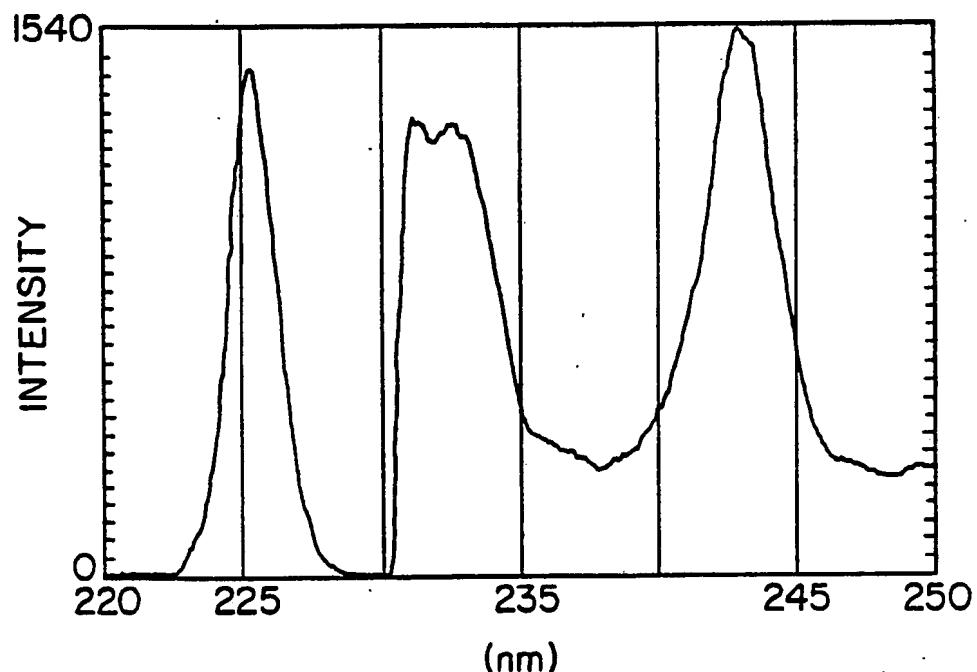

Fig. 20

Fig. 21

Fig. 22

INTERNATIONAL SEARCH REPORT

International Application No **PCT/US 88/03257**

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) *

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC4: A 61 B 1/06

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC4	A 61 B, G 02 B, G 01 J

Documentation Searched other than Minimum Documentation
to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
A	US, A, 4494823 (YOSHIDA ET AL) 22 January 1985, see column 1, line 5 - column 2, line 9; column 5, line 17 - line 43; abstract; figures 1,6 --	1-10
A	US, A, 4163148 (FRITSCHE ET AL) 31 July 1979, see the whole document --	1-10

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* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

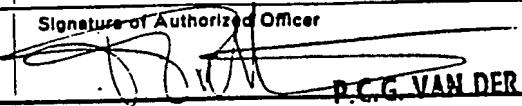| Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
7th February 1989	0 6 MAR 1989

International Searching Authority	Signature of Authorized Officer
EUROPEAN PATENT OFFICE	P.C.G. VAN DER PUTTEN

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The members are as contained in the European Patent Office EDP file on   12/01/89
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A- 4494823	22/01/85	EP-A-B- 0081192 JP-A- 58153911 CA-A- 1204313	15/06/83 13/09/83 13/05/86
US-A- 4163148	31/07/79	DE-A- 2708507 JP-A- 53125053 CH-A- 629603	31/08/78 01/11/78 30/04/82